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A NOVEL TEST FOR IVF MISCARRIAGE RISK: ANNEXIN A5 M2 HAPLOTYPING IN IVF PATIENTS AND PREIMPLANTATION EMBRYOS

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INTRODUCTION

The anticoagulant protein Annexin A5 (ANXA5), helps maintain placental vasculature. The M2 haplotype of the *ANXA5* promoter results in decreased protein levels affecting placental vasculature and is associated with increased risk of miscarriage and other placental mediated pregnancy complications. Low dose heparin treatment is an effective strategy to improve IVF success rates in M2 carrier patients from 16% to 42% clinical pregnancy rate (Fishel et al. EBioMedicine. 2016). M2 testing is limited to cumbersome phlebotomy and sanger sequencing and is unavailable in preimplantation embryos.

OBJECTIVE

To develop a new test for evaluating M2 carrier status in IVF patient saliva and preimplantation embryos.

METHODS

Test performance was measured by comparing Sanger sequencing on parental blood DNA and quantitative real-time (q)PCR on saliva DNA, cell line 7-cell replicates, cell line 7-cell samples and corresponding purified DNA, trophectoderm biopsies and DNA isolated from the corresponding embryonic stem cell line, Mendelian inheritance expectations in embryos, embryo sanger sequencing, and SNP microarray-based linkage analyses.

RESULTS

M2 saliva qPCR. 100% concordance was obtained between conventional sanger sequencing and a novel qPCR method on saliva DNA.

M2 PGT validation. 100% concordance was obtained between all replicates of cell line 7-cell and corresponding bulk DNA samples.

M2 trophectoderm PGT. 100% concordance was obtained between qPCR and Mendelian inheritance with SNP array based linkage analysis in human blastocyst biopsies (n=107).

Figure 1. Example saliva DNA sample results.

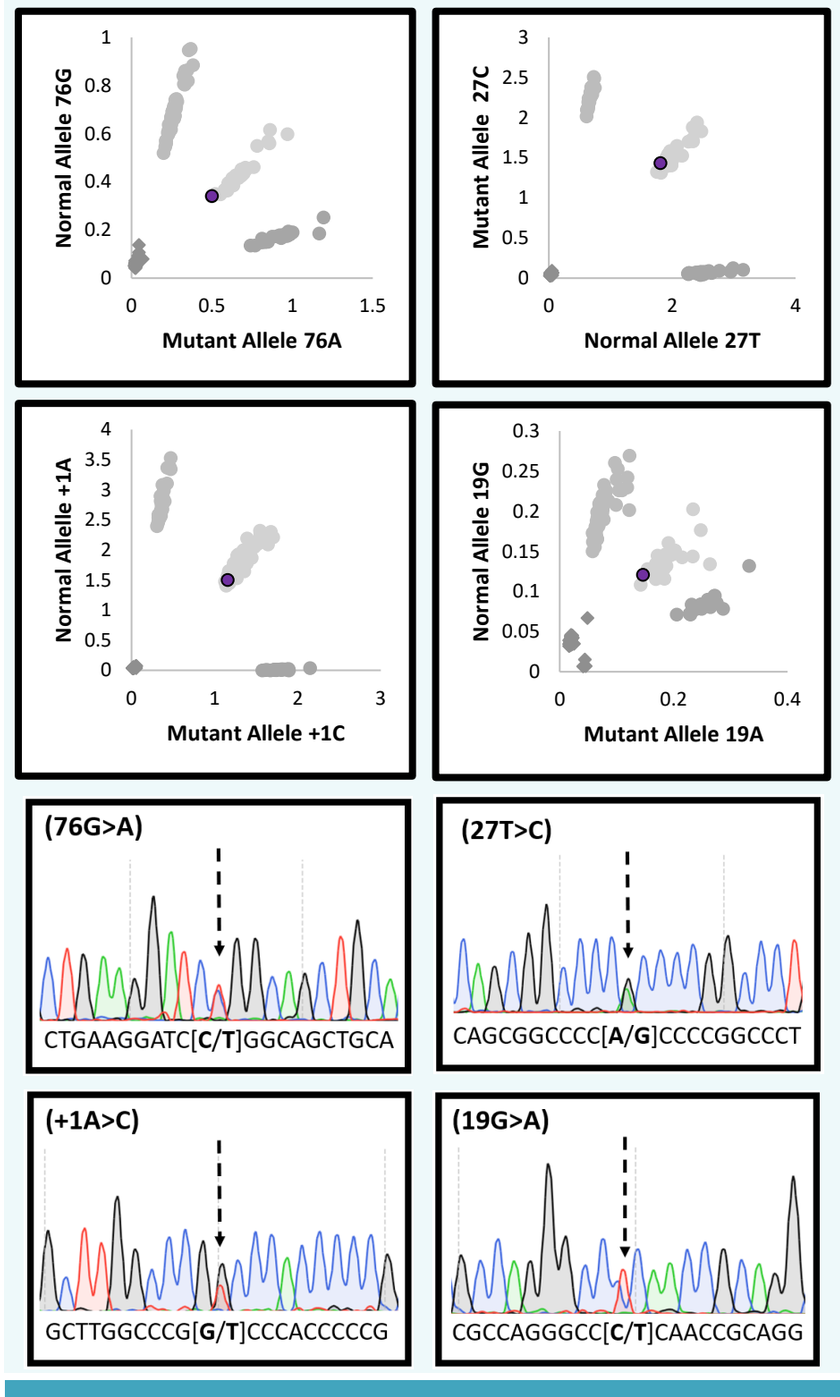


Figure 2. Example 7-cell sample results.

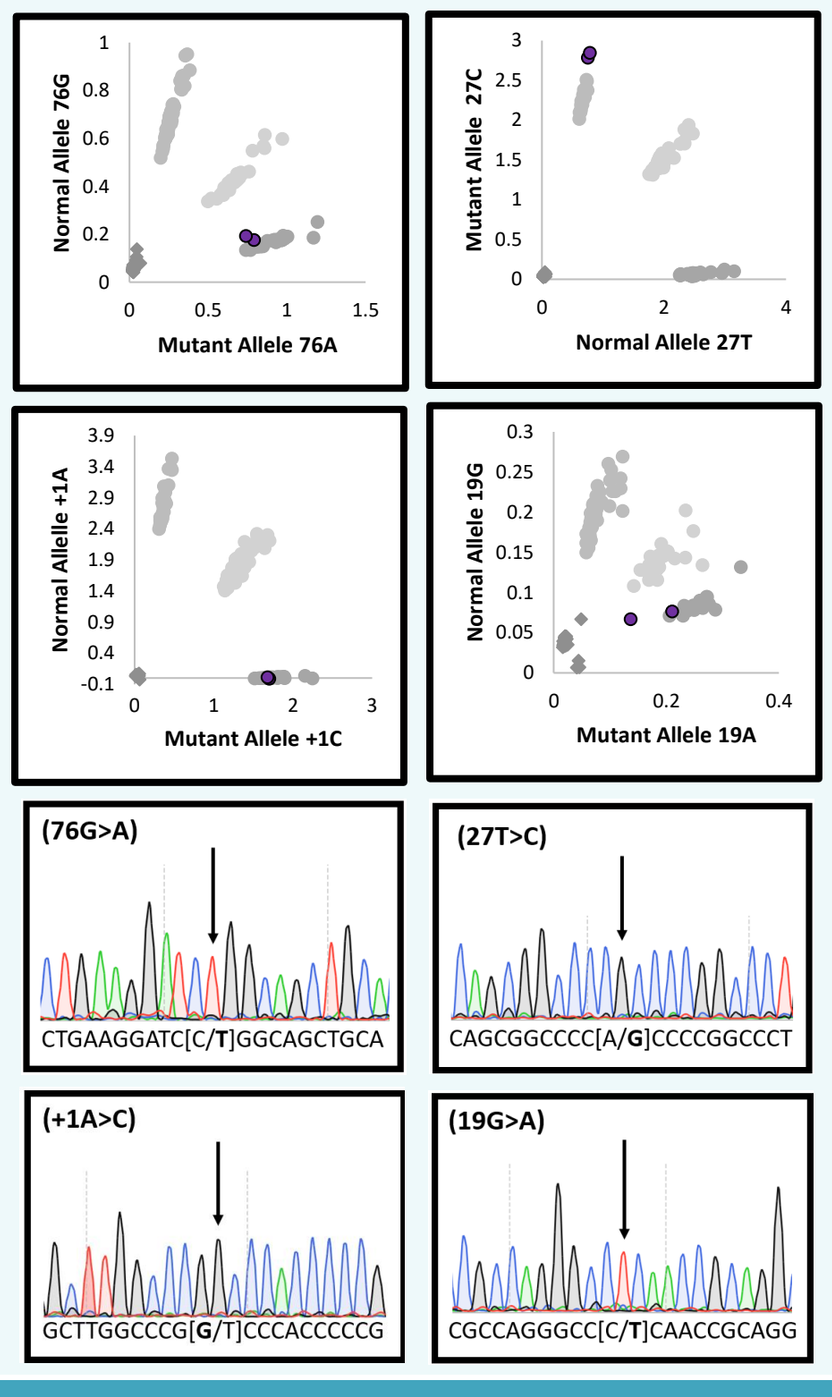
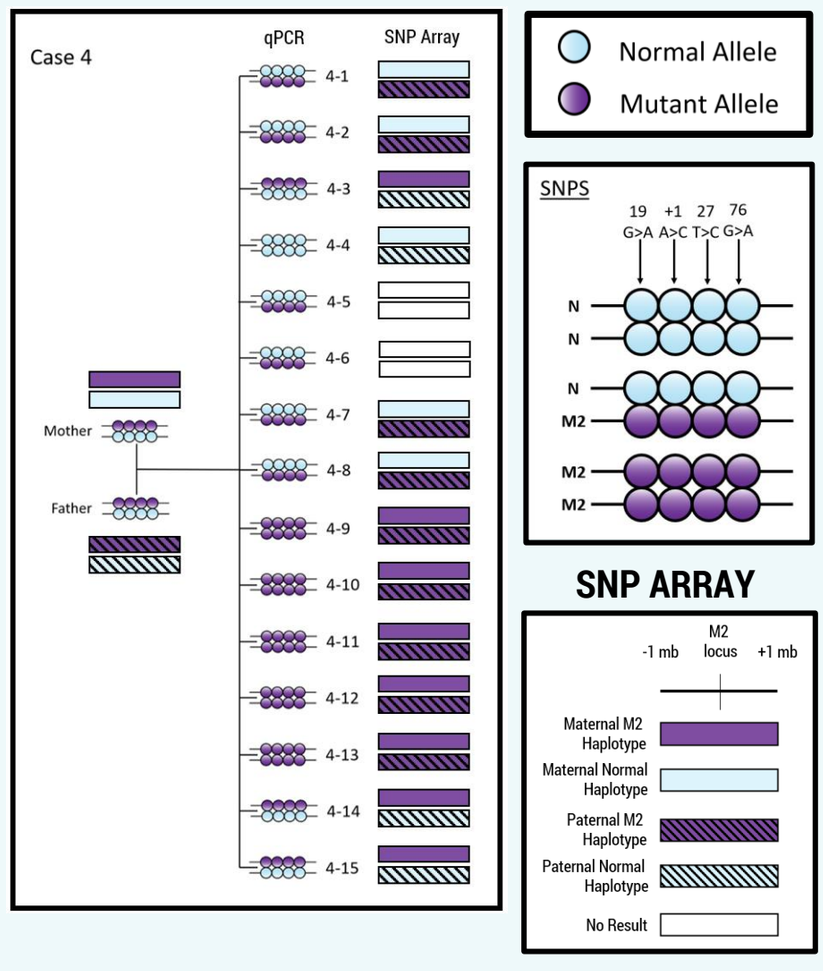


Figure 3. Example PGT case.



CONCLUSIONS

We have developed and validated a saliva DNA-based M2 haplotyping test for infertile patients, and a new ability to perform “PGT-M2 haplotyping” for carrier couples undergoing IVF. Future work will include prospective analysis of clinical outcomes following embryo selection and non-selection with PGT for M2 carrier status.